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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Kirsch, et al.	Group Art Unit 6247
Appl. No.	:	09/924,396	
Filed	:	August 6, 2001	
For	:	IRON REGULATING PROTEIN-2 (IRP-2) AS A DIAGNOSTIC FOR NEURODEGENERATIVE DISEASE	
Examiner	:	Chernyshev, Olga N	

DECLARATION UNDER 35 C.F.R. §1.132

United States Patent and Trademark Office
P.O. Box 2327
Arlington, VA 22202

Dear Sir:

1. This Declaration is being submitted to demonstrate that the claimed invention can be used for both Alzheimer's Disease (AD) and Parkinson's Disease (Parkinsons) and that it will work to diagnose and identify a predisposition for such diseases by using any sample containing peripheral blood cells.

2. My name is Wolff M. Kirsch, M.D., and I am an inventor on the above-identified patent application and am familiar with the prosecution history .

3. I have extensive experience in the field of neurobiology as evidenced by my attached curriculum vitae (Exhibit A) and I have been practicing and doing research in the field of Neurobiology for approximately 40 years.

4. Prior to the present invention, both AD and Parkinsons have been notoriously difficult to diagnose. They typically require hours of extensive cognitive, psychometric, and physical tests which serve to identify the presence of AD and/or Parkinsons, and rule out the

possibility of other diagnoses. These tests are the most reliable in later stages of the diseases when phenotypic/behavioral changes can be seen. Thus, the invention, which provides a non-invasive method of diagnosis using molecular signs of disease is needed to reduce the time and expense as well as the patient discomfort associated with the psychometric tests. This, however, brings home the fact that compared to hours of analysis by a Neurobiologist, a simple lab test on a patient sample, would be a clear improvement to the cost, the patient comfort, and the Doctor's time.

5. The enclosed immunocytochemistry micrograph (exhibit B) provides strong evidence that peripheral blood cells can be used to identify the abnormal levels of IRP-2 produced by AD patients. The micrograph shows that lymphocytes stained with IRP-2 antibodies produce a clearly different pattern for Alzheimer's patients as compared to controls. This data was obtained following the enclosed protocol (exhibit C). The patient used in the study was diagnosed as shown in the attached exhibit D. Exhibit D contains 11 pages of tests which were performed on the Alzheimer's patient in 1992-1993 to identify the symptoms of Alzheimers and to rule out any other possible causes of such symptoms. The tests included liver tests, blood tests (SGOT is a metabolic test), MRI, EEG, and CT of brain to rule out brain tumor and stroke, and a physical assessment (see page 7 of the geriatric assessment) to rule out other causes. The geriatric assessment concluded that the patient had mild cognitive impairment. Subsequent tests have confirmed the diagnosis and the disease has now progressed to full AD. The patient is now living in a home and requires constant supervision due to the progression of the disease.

6. Thus, the immunocytochemical data is incontrovertible evidence that diagnosis of AD can be made using patient samples containing peripheral blood cells even at a very early stage in the disease. Further, the ability to use blood to diagnose Alzheimers disease is further supported because the activity of blood cells has been identified to be altered in AD. See the enclosed Grant Application (Exhibit E), page 44, section B.2.2 which reads as follows:; "In determining whether ex vivo markers for AD can be found in the peripheral blood, it should be noted that there is convincing evidence pointing to the fact that the biological activity of peripheral blood lymphocytes, platelets and macrophages can be affected in patients with AD.".

7. The method of diagnosis using IRP-2 levels can also be used to diagnose Parkinsons. Parkinson's disease is also associated with abnormal levels of iron. The enclosed references (Exhibits F and G) show that there is a considerable belief in the field that the aspect

of Alzheimer's and Parkinson's disease which results in increased levels of iron can be traced to a common pathway, if not to a common etiology. The abnormal IRP-2 levels lead to abnormal iron regulation. For example, antibodies specific to IRP-2 will identify any cells which are expressing an abnormal amount of IRP-2.

8. Applicants' invention was based, at least in part, on the discovery that abnormal levels of IRP-2 protein could be identified in peripheral blood cells. The data obtained from AD patients can also be extended to Parkinsons in view of the abnormal levels of IRP-2 known to be found in neural tissue from Parkinsons patients. Based on Applicant's discovery that IRP-2 levels can be identified in samples containing peripheral blood cells, the abnormal levels of IRP-2 associated with Parkinsons could also be identified in samples containing peripheral blood cells from Parkinsons patients.

9. Once abnormal levels of IRP-2 are identified, an analysis of the patient's symptoms can be used to distinguish AD from Parkinsons or other neurodegenerative disease. The claimed invention will be a powerful diagnostic aid for the diagnosis and predisposition to AD and/or Parkinsons.

10. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 Title 18 of the United States code and that such willful, false statements may jeopardize the validity of the application or patent issuing therefrom.

Dated: 6/5/03

Wolff M. Kirsch, M.D.

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